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Outcome of patients with repeat peritonitis in peritoneal dialysis: 3 case reports

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Abstract. *Peritonitis is one of the most common and serious complications of peritoneal dialysis (PD), significantly impacting the survival of the peritoneal membrane and, consequently, the overall success of dialysis. Repeat peritonitis, defined as the occurrence of another episode of peritonitis more than four weeks after the completion of treatment for a prior episode, often requires catheter removal. The most frequent pathogens involved are skin-related, such as Staphylococcus aureus and coagulase-negative Staphylococcus, though other bacteria like Escherichia coli (E.coli) and Serratia marcescens (SM) also pose significant risks, especially with recurrence and poor prognosis. We report three cases of repeat peritonitis due to different pathogens, which ultimately led to the removal of the PD catheter. The first case involved a 45-year-old female with repeat E.coli and SM infections. Despite antibiotic treatment, her peritonitis recurred, leading to catheter removal. The second case featured a 17-year-old female with repeat SM infection, where treatment included catheter removal and successful replacement. The last one described a 74-year-old male with multiple episodes of peritonitis caused by Staphylococcus species, culminating in severe complications, including Candida superinfection, requiring both catheter removal and transition to hemodialysis. These cases highlight the challenges in managing repeat peritonitis and emphasize the importance of timely catheter removal in preventing further complications and improving patient outcomes. Moreover, they underline the need for comprehensive monitoring and appropriate antimicrobial therapy in preventing recurrent peritonitis in PD patients.*

Keywords: *repeat peritonitis; peritoneal dialysis; catheter removal; hemodialysis*

Introduction

Peritoneal dialysis (PD) peritonitis is the most common and serious complication of PD. It can lead to severe anatomical changes in the peritoneum, limiting the viability of the peritoneal membrane and thereby affecting dialysis exchanges [1].

Repeat peritonitis is defined as the occurrence of a peritonitis episode more than four weeks after the completion of treatment for a previous episode, caused by the same organism or a sterile (culture-negative) episode [2].

The most common pathogens responsible for repeat peritonitis, sometimes requiring the removal of the PD catheter, are of skin origin: *Staphylococcus aureus* and coagulase-negative *Staphylococcus* [3].

However, other bacteria pose serious risks due to their prognosis and recurrence, particularly infections caused by *SM* and *E.coli*, as they are associated with a higher risk of technique failure and mortality [4].

We report three cases of repeat peritonitis caused by different germs, which required the removal of the PD catheter.

Case report 1

This case concerns a 45-year-old female patient undergoing continuous ambulatory PD (CAPD) for three years due to end-stage chronic kidney disease secondary to polycystic kidney disease. She is registered on the national kidney transplant list for a deceased donor transplant.

The patient is autonomous and has a Charlson score of 2. She is well-monitored and stable (with a nPcr > 0.8), achieving adequate dialysis clearance and fluid-electrolyte balance (optimal Kt/V > 2.5 and CHC > 55 ml/min). She maintains a urine output of approximately 3 liters per

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day, indicating good residual renal function (greater than 7.5 ml/min).

She developed her first Gram-negative peritonitis (*Enterobacter cloacae*) in February 2021, two months after PD catheter placement. It was treated based on the antibiogram with a single dose of gentamicin (5 mg/kg), ceftazidime (1 g/day), and ciprofloxacin (500 mg/day) for three weeks, with a favorable outcome.

In September 2022, she developed a second peritonitis episode, occurring long after the first. Cytobacteriological analysis of the dialysis fluid identified *E.coli*, which was treated with two doses of amikacin (1 g) and ceftriaxone (1 g/day) intraperitoneally for three weeks.

One month after completing her antibiotic therapy, she experienced a third episode of peritonitis caused by the same pathogen (*E.coli*), classified as repeat peritonitis. This was treated with two doses of gentamicin (5 mg/kg) and ceftazidime (1 g/day) intraperitoneally for three weeks, with good clinical and biological improvement.

At the end of December 2022, two months after her last peritonitis episode, she presented with cloudy dialysis fluid but remained asymptomatic. Clinically, she was stable. Laboratory findings indicated an inflammatory syndrome: leukocytosis (12,100 cells/mm^3) with a predominance of neutrophils (11,100 cells/mm^3) and a C-reactive protein (CRP) at 47 mg/L.

Cytobacteriological analysis of the dialysate revealed 12,400 leukocytes/mm^3 (90 % neutrophils, 10 % lymphocytes), and culture identified *E.coli* and *SM*, both sensitive to ceftazidime. Aerobic and anaerobic cultures confirmed the presence of *E.coli*.

The initial treatment consisted of intraperitoneal ceftazidime (1 g/day), cefazolin (1 g/day), and a single dose of amikacin (1 g). Then, per international recommendations, therapy was adjusted to intraperitoneal ceftazidime (1 g/day) and ciprofloxacin (500 mg/day) for three weeks based on the antibiogram.

Clinically and biologically, the patient showed a favorable response to antibiotic therapy, with the dialysis fluid clearing after four days of treatment.

To investigate the underlying cause of her recurrent Gram-negative peritonitis, digestive tract evaluations were conducted but did not reveal any local cause of bacterial overgrowth:

— A digestive fibro-colonoscopy (performed under appropriate antibiotic prophylaxis) showed no diverticulosis or digestive polyps but revealed left colonic angiodysplasia without metaplasia or dysplasia.

— A biopsy identified antral and fundic gastritis due to *Helicobacter pylori*, for which she was treated with metronidazole, amoxicillin, and clarithromycin for 15 days.

— An abdominal angio-CT scan revealed enlarged kidneys (20 × 11 × 6 cm) with some renal cystic hemorrhages but no signs of cyst infection.

Given the recurrence of these intestinal pathogens and after expert consultation, the PD catheter was removed. The patient was transitioned to hemodialysis since her peritonitis was not resolved by antibiotic treatment alone.

Case report 2

This case concerns a 17-year-old female patient who has been undergoing automated PD (APD) since the age of 11 (in 2016) due to reflux nephropathy. She is well-monitored and stable (with a good nPCR), achieving adequate dialysis clearance (optimal Kt/V and CHC) and has a Charlson score of 2. She is autonomous.

She is also registered on the national kidney transplant list for a deceased donor transplant.

In February 2022 (six years after PD catheter placement), she developed her first episode of peritonitis caused by *SM*. Treatment was guided by the antibiogram and consisted of two doses of gentamicin (7 mg/kg) and intraperitoneal ceftazidime (1 g/day) for three weeks. The evolution was marked by good clinical and biological improvement.

Two months later (April 2022), she was admitted for repeat peritonitis caused by the same pathogen (*SM*). Treatment, based on the antibiogram, included two doses of gentamicin (7 mg/kg) and intraperitoneal ceftriaxone (1 g/day) for three weeks. The patient showed good clinical and biological improvement.

Four months after her second peritonitis episode, she presented with abdominal pain, vomiting without diarrhea, and cloudy dialysate for three days.

Clinically, she was stable but showed an hyperleukocystosis (16,100 cells/mm^3), with a CRP at 118 mg/L.

Bacteriological analysis of the dialysate showed 4,370 leukocytes/mm^3 (90 % neutrophils, 10 % lymphocytes), and culture confirmed the presence of *SM*, sensitive to ceftazidime. Aerobic and anaerobic cultures identified the same pathogen.

The patient initially received empirical treatment with intraperitoneal ceftazidime (1 g/day), cefazolin (1 g/day), and a single dose of amikacin (1 g). Subsequently, only intraperitoneal ceftazidime (1 g/day) was maintained according to the antibiogram.

The clinical course showed regression of abdominal pain and vomiting after two days and clearing of the dialysate fluid after five days of antibiotic therapy.

Since this was the third episode of peritonitis caused by the same pathogen, and based on the medical literature, the PD catheter was removed, and a new catheter was simultaneously placed on the contralateral side.

Cytobacteriological and parasitological examinations of the external and internal Dacron cuffs, as well as the catheter tip, did not reveal any microorganisms. Histopathological examination of the peritoneum showed no abnormalities.

Four days after catheter placement, APD was gradually resumed with low initial fill volumes.

The patient has not experienced any further peritonitis episodes to date, with a follow-up of one year.

Case report 3

This case concerns a 74-year-old retired nurse with end-stage chronic kidney disease secondary to diabetic nephropathy. He has been undergoing APD since 2021 and has a Charlson score of 8. He is autonomous and in good general condition.

He maintains a urine output between 1.5 and 2 liters, with a residual renal function of 8 mL/min and good dialysis adequacy (optimal Kt/V and CHC).

Six months after PD catheter placement, he experienced his first episode of peritonitis caused by coagulase-negative *Staphylococcus*, which was treated with intraperitoneal cefazolin (1 g/day) and a single dose of gentamicin (7 mg/kg), leading to rapid improvement.

Seven months later, he developed a second episode of peritonitis caused by coagulase-negative *Staphylococcus* and *E.coli*, treated with intraperitoneal ceftazidime, ciprofloxacin, and a single dose of gentamicin (7 mg/kg).

A year later, he presented with a third episode of peritonitis due to *Enterobacter cloacae*, treated with ceftriaxone (1 g/day) for 21 days, followed by a fourth recurrent peritonitis caused by coagulase-negative *Staphylococcus*, managed with intraperitoneal cefazolin (1 g/day) for 15 days.

Two months later, he developed a fifth episode of peritonitis due to *Staphylococcus epidermidis* and methicillin-resistant coagulase-negative *Staphylococcus*, treated with cefazolin (1 g/day) and ciprofloxacin (500 mg/day) for two weeks.

Six days after discontinuing antibiotic therapy, he reported mild abdominal pain and dizziness, without fever. Laboratory findings showed an hyperleukocytosis (10,100/mm^3), and a CRP at 27 mg/L.

Cytocultures confirmed a sixth peritonitis episode caused by *Staphylococcus haemolyticus*, for which he was treated with intraperitoneal vancomycin. However, the clinical course worsened, with cloudy dialysis fluid appearing after 11 days of antibiotic therapy. Cytobacteriological and parasitological analyses revealed a superinfection of the dialysate fluid with *Candida parapsilosis* and *Staphylococcus haemolyticus*. The patient was subsequently started on fluconazole and ceftazidime. To prevent further recurrences and potentially fatal complications, the PD catheter was removed, and the patient was referred to hemodialysis.

Discussion

Peritonitis is a major cause of treatment failure in patients undergoing PD. It is secondary to an infection caused by gram-positive or gram-negative bacteria. It can be monomicrobial or polymicrobial (particularly in the case of *E.coli* infection) [5, 6].

These episodes of peritonitis are more severe because they cause significant harmful changes to the peritoneal membrane, which negatively impacts the survival of PD and increases mortality [7].

Staphylococcus (both coagulase-negative and *aureus*) is a gram-positive cocci and is the most frequent cause of relapsing and/or repeat peritonitis related to PD, often exacerbated by poor hygiene [1].

Methicillin resistance is common, but the treatment outcome remains favorable when cefazolin is used as the first-line antibiotic, with clinical improvement and rapid clearing of the dialysate fluid in the first days of treatment [8, 9].

E.coli is a gram-negative bacillus known to be part of the commensal intestinal flora but can also cause intestinal and extraintestinal diseases. It is responsible for a significant proportion of monomicrobial enterobacterial PD-peritonitis patients [5].

Outside the intestinal tract, where it is not virulent, *E.coli* can cause urinary tract infections, pneumonia, bacteremia, catheter-related infections, and peritonitis [10]. Several studies have reported variable virulence factors for this pathogen: the individual characteristics of the affected patient (age, race, nutritional status, comorbidities) and the virulence factors of the specific strain involved can determine the outcome of peritonitis [11, 12].

Unlike other gram-negative organisms that have a poor prognosis (such as *Pseudomonas* or *Klebsiella*), the outcomes of peritonitis in PD patients caused by *E.coli* vary, ranging from relatively favorable results to higher incidences of treatment failure and catheter removal [6, 13], as shown in our first case study.

In contrast to the previous common pathogen, *SM* is a rare, opportunistic, gram-negative bacterium that is also part of the Enterobacteriaceae family. It is commonly found in the urinary, gastrointestinal, and respiratory tracts. The main risk factors for *SM* bacteremia include hospitalization, insertion of intravenous catheters, PD catheters, urinary catheters, and respiratory tract instrumentation. It is associated with urinary and respiratory infections, sepsis, endocarditis, osteomyelitis, ocular infections, and meningitis [14–17]. This bacterium is difficult to treat due to its intrinsic resistance to certain antimicrobials and is associated with poorer outcomes compared to other gram-negative bacteria. A key feature of *SM* is its ability to produce beta-lactamase, which confers resistance to broad-spectrum antibiotics. It is generally resistant to ampicillin, tetracycline, cefazolin, cephalothin, and cefuroxime [18, 19]. It is sensitive *in vitro* to the third-generation cephalosporins, but monotherapy exposes the risk of selection of resistant mutants and its combination with an aminoglycoside could also lead to therapeutic failure through mutant selection. Combination with fluoroquinolones is then recommended as a means of avoiding the selection of mutants resistant to third-generation cephalosporins, and the risk of selection is absent or greatly reduced with fourth-generation cephalosporins (cefepime, cefpirome) which are not hydrolyzed by cephalosporinases, whatever their level of production. Another alternative could be meropenem [20].

These three observations highlight the difficulty in managing peritonitis that reoccurs despite appropriate antibiotic treatment, likely due to the formation of a biofilm. We suggest that catheter removal should be considered in repeat and relapse PD-peritonitis cases, which will help control the infection and prevent septicemia, while permanent transfer to hemodialysis must be discussed on a case-by-case basis.

Conclusions

PD-peritonitis is the most frequent infectious complication, and antibiotics alone may not be sufficient to prevent recurrences and relapses. The removal or replacement of the PD catheter helps control the infection, prevent infectious complications and the loss of the PD technique.

Primary prevention (particularly retraining of patients and medical and nursing staff) and secondary prevention, as

well as the search for a local cause, are necessary to preserve the quality of the peritoneal membrane and prolong the survival of the PD technique [21].

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Результати лікування пацієнтів із повторним перитонітом при перитонеальному діалізі: звіт про 3 випадки

Резюме. Перитоніт є однім із найбільш поширених та серйозних ускладнень перитонеального діалізу (ПД), що значно впливає на виживання перитонеальної мембрани та, відповідно, загальний успіх діалізу. Повторний перитоніт, визначений як виникнення іншого епізоду перитоніту через більше ніж чотири тижні після завершення лікування попереднього епізоду, часто потребує видалення катетера. Найбільш поширеними патогенами є шкірні бактерії, як-от *Staphylococcus aureus* та коагулазонегативні стафілококи, хоча інші бактерії, наприклад *Escherichia coli* (*E.coli*) та *Serratia marcescens* (*SM*), також становлять значну загрозу, особливо при рецидивах і поганому прогнозі. Повідомлено про три випадки повторного перитоніту, спричиненого різними патогенами, що в кінцевому підсумку призвело до видалення ПД-катетера. Перший випадок стався в 45-річної жінки з повторними інфекціями *E.coli* та *SM*, у якій, незважаючи на антибіотикотерапію, перитоніт рецидивував, що призвело до видалення катетера. Другий випадок стосувався 17-річної пацієнтки з повторною інфекцією *SM*; лікування включало видалення катетера та успішну його заміну. Останній випадок описує 74-річного чоловіка з численними епізодами перитоніту, спричиненими різними видами *Staphylococcus*, що призвело до тяжких ускладнень, зокрема кандидозної суперінфекції, і потребувало як видалення катетера, так і переходу на гемодіаліз. Ці випадки підкреслюють труднощі в лікуванні повторного перитоніту й важливість своєчасного видалення катетера для запобігання подальшим ускладненням і поліпшення результатів для пацієнтів. Крім того, вони акцентують необхідність комплексного моніторингу та належної антибактеріальної терапії для запобігання рецидивам перитоніту в пацієнтів, які проходять ПД.

Ключові слова: повторний перитоніт; перитонеальний діаліз; видалення катетера; гемодіаліз